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Results of a national survey among Dutch surgeons treating patients with colorectal carcinoma. Current opinion about follow-up, treatment of metastasis, and reasons to revise follow-up practice

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Abstract

Objective Follow-up after curative resection of colorectal carcinoma (CRC) has been subjected to debate concerning its effectiveness to reduce cancer mortality. Current national and international guidelines advise CEA measurements every 3 months during 3 years after surgery. The common clinical practice and opinion about follow-up for colorectal carcinoma, was evaluated by means of a survey among Dutch general surgeons.

Method A web-based survey of follow-up after treatment of CRC was sent to all registered Dutch general surgeons. A reply from 246 surgeons treating patients for colorectal carcinoma in 105 out of 118 hospitals was received (response rate 91%). Questions related to actual follow-up protocol, opinion about serum CEA monitoring, liver and/or lung metastasectomy, and motivation to participate in a new trial concerning follow-up.

Results For the majority of surgeons the length of follow-up was influenced by age of the patient (62%) and

physical condition (76%) prohibiting hepatic metastasectomy. The generally accepted follow-up protocol consisted of CEA measurements every 3 months in the first year and six-monthly thereafter, and ultrasound examination of the liver every 6 months. Nearly all surgeons (92%) were willing to participate in a new study of follow-up protocol.

Conclusion The adherence to national guidelines for the follow-up of colorectal carcinoma is low. The indistinctness about follow-up after curative treatment of colorectal carcinoma also affects clinical practice. Recent advancements in imaging techniques, liver and lung surgery have changed circumstances, which are not yet anticipated upon in current guidelines. Renewal of follow-up based upon scientific evidence is required.

Keywords colorectal neoplasms, oncology, carcino-embryonic antigen, follow-up

Introduction

There is controversy regarding follow-up after curative resection of colorectal carcinoma (CRC) regarding its effectiveness in reducing cancer mortality. No clinical trial or meta-analysis has unequivocally shown a benefit on patient survival [1–6]. In the past 30 years, several attempts have been made to improve survival, either by advancements in treatment or changing the protocol of follow-up. Only serum CEA has proven to be of (limited) value, with consistent results on lead time but

inconsistent results on survival [1,7–17]. Current guidelines [18–22] therefore advise CEA measurement every 3 months over 3 years. To detect metachronous second colorectal malignancy, colonoscopy is advised every 3 years [20]. Dutch guidelines are similar to those advised by the American Society of Clinical Oncology. The lack of solid evidence on the benefit of follow-up has raised the question whether follow-up should be continued. Technical developments in imaging and increased use of liver and lung surgery for metastatic disease outdate present guidelines since they still reflect the results from studies that were done before these developments.

A survey was undertaken among Dutch general surgeons treating patients with colorectal carcinoma to

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assess the opinion on diagnostic methods used in follow-up, the adherence to national guidelines concerning CEA measurement, and the treatment of recurrent disease. The motivation of the respondents to participate in new studies concerning follow-up was also evaluated.

Method

A request to complete a web-based survey was sent to all registered general surgeons in the Netherlands ($n = 878$). A reply was received from 246 surgeons treating patients with colorectal carcinoma from 105 different hospitals out of a total of 116 hospitals in the Netherlands with a surgical department, giving a response rate of 91%.

To detect possible bias through differences in response rate within hospitals, the outcome was also calculated using only one representative per hospital. In comparison with the outcome from all 246 surgeons, there were no differences.

The survey included 17 questions, with a total of seven free answers that were categorized afterwards. They related to the indication for follow up, actual local follow-up practice, application of serum CEA measurement and opinion about serum CEA monitoring in follow up. The use and availability of other diagnostic methods, both for screening and evaluation of suspected metastases, and practice concerning treatment of liver and lung metastases were evaluated. Finally the opinion and feasibility for a new study, in response to a proposition in the questionnaire, was sought.

Results

Each surgeon treated approximately 30 patients with CRC per year. The length of follow up was influenced by age according to 62% ($n = 153$) and physical condition

prohibiting hepatic metastasectomy according to 76% ($n = 187$). Usually after the age of 80 years follow-up was limited.

In Table 1, the percentage of surgeons who adhered to a certain follow-up test at a specific moment is given. In general CEA was measured with a lower intensity than guideline advice, especially in the second and third year, and ultrasound was used regularly. Colonoscopy was regularly done in year 1, 3 and 5 and one-third requested a yearly chest X-ray.

The majority of surgeons (65%, $n = 161$) used the thresholds for the CEA value as suggested in the questionnaire as follows: CEA < 5 ng/ml: no action, CEA > 5 < 10 ng/ml: monthly measurement, evaluation for recurrent disease when CEA is rising, CEA > 10 ng/ml: evaluation for recurrent disease. CEA was not measured at all by 6% of respondents, CEA-rise or doubling time was used by 14%, a lower threshold was applied by 7% and a higher threshold by 2%. The majority (67%) chose helical computed tomography (CT) scanning of the chest and abdomen for evaluation of suspected recurrent disease, followed by positron emission tomography (PET) scanning when nothing is found on CT. Ultrasound was added by 11% of surgeons and colonoscopy by 4%.

A one-third of surgeons (31%) treating colorectal carcinoma carried out liver resections as well. Analysis of the opinion concerning the eligibility criteria for hepatic metastasectomy was done for the whole group and separately for the liver surgeons. A large majority of all surgeons (93%) concurred with liver and lung resections for metastasectomy. A minority (27%) did not consider liver resection indicated when resectable extrahepatic disease was present. There is no disagreement on these two criteria among the general and liver surgeons. Liver surgeons expressed a different opinion on the eligibility for hepatic metastasectomy when lymph node

Table 1 Follow-up scheme, current practice.

Year	1				2				3				4		5	
Month	3	6	9	12	3	6	9	12	3	6	9	12	6	12	6	12
Physical examination	89	78	50	78	17	72	16	74	3.7	49	4.5	74	30	55	26	66
CEA	63	78	50	83	20	69	20	78	8	47	8	74	28	60	25	67
Ultrasound liver	11	44	10	58	4	36	3.3	56	2	22	2.8	48	8.5	36	7.3	44
Chest X-ray	5	18	5	32	0.4	13	0.4	29	–	8	1.2	26	3.6	19	3.3	25
Colonoscopy	2	7	1.6	65	2	5	–	16	3	2.4	7.7	38	5.3	18	2.8	35
CT abdomen	1.2	2.4	0.4	8	0.4	2.4	0.4	4.5	0.4	1.2	0.4	4.5	0.8	2.4	0.4	3.7
CT thorax	–	0.8	0.4	4	0.4	0.8	0.4	0.8	0.4	–	0.4	0.8	0.4	0.8	0.4	0.8

In each box the percentage of surgeons that carries out the examination at that time, is given. All percentages >35% are in italics, all percentages between 15 and 35% are in bold and beneath 15% are in bold italics.

Table 2 Eligibility for hepatic metastasectomy.

	All surgeons (<i>n</i> = 246) (%)	Liver surgeons (<i>n</i> = 76) (%)
Macroscopic resectable metastasis	96.1	98.6
Bilobar localization	81.6	96.1
Lymph node metastasis in the hepatoduodenal ligament	17.3	33.3
Resectable extrahepatic disease	73.2	68.4
Resectable lung metastasis	92.6	88.2
Number of metastasis is a criterion	23.5	19.7

involvement in the hepatoduodenal ligament and bilobar disease were present. They considered these findings to be less often a contraindication for surgery (Table 2). The majority of surgeons (76%) felt that the number of metastases was not a decisive criterion for metastasectomy. When the number of metastases was considered important, a maximum of three to five was generally regarded as being amenable to surgery.

Nearly all surgeons (92%) were willing to participate in a new study concerning follow-up. When imaging was added to the proposed new follow-up scheme, ultrasound was preferred above CT scan of the abdomen by general surgeons. When the results were analysed for surgeons who also perform liver surgery, CT scanning was preferred above ultrasound. Generally imaging every

6 months in the first 2 years and every year in years three, four and five was supported by the respondents (Table 3). The most important exclusion criteria for metastasectomy included age and physical condition.

Discussion

The results of this survey are highly representative for the current follow-up after surgical treatment for patients with colorectal cancer in the Netherlands. The high response rate is likely due to the easy accessibility of the survey on the web, and the present interest in surgery for metastases. The results of this survey reflect the doubts and uncertainty in follow-up and treatment options for recurrent disease.

Age and poor physical condition are the main reasons which limit follow-up. At least a quarter of surgeons did not consider that age or physical condition should limit follow-up. Frequently expressed arguments for continuing regular outpatient visits include quality control of surgical treatment and psychosocial considerations. Both arguments are controversial [23–26].

The median time after which recurrent disease is detected (disease free interval) is approximately 0.5–2 years for liver metastasis, 2–3 years for lung metastasis and 0.5–1.5 years for local recurrence [10,11,14,17,27–29,31–34]. The time after which metastasis or local recurrence are diagnosed varies with the diagnostic methods used [14,15,29–32] and the detection of local recurrence might also be dependent on the site of the primary tumour (colon or rectum). The common practice

Table 3 Suggested imaging (all surgeons).

Year	1				2				3				4		5	
Month	3	6	9	12	3	6	9	12	3	6	9	12	6	12	6	12
Ultrasound	17	54	14	57	4.9	40	4.1	57	1.6	26	2.4	51	11	35	10	46
Ct abdomen	3.3	27	1.6	50	1.2	22	1.2	42	1.6	7.3	2.0	30	4.1	16	4.1	25

In each cubicle the percentage of surgeons that carries out the examination at that time, is given. All percentages >35% are in italics, all percentages between 15 and 35% are in bold and beneath 15% are in bold italics.

Table 4 Suggested imaging (liver surgeons).

Year	1				2				3				4		5	
Month	3	6	9	12	3	6	9	12	3	6	9	12	6	12	6	12
Ultrasound	19	43	20	32	4.1	26	4.1	39	1.4	22	1.4	30	9.5	23	8.1	28
CT abdomen	4.1	39	1.4	65	1.4	35	1.4	54	1.4	6.8	1.4	28	5.4	15	4.1	20

In each cubicle the percentage of surgeons that carries out the examination at that time, is given. All percentages >35% are in italics, all percentages between 15 and 35% are in bold and beneath 15% are in bold italics.

concerning CEA measurement, despite the recommendation in national guidelines, limited the three monthly measurements to the first year. After that the intensity of controls diminished to every 6 months or longer. Actual measurement was often even lower and never more than 50% for CEA measurement at each moment (Grossmann I, unpublished results). Thus the present clinical practice does not anticipate the actual moment recurrent disease appears. This might lead to missing more potentially curable recurrent disease than is necessary. The logistic burden of follow-up might be another reason for the low adherence to guidelines as others have reported [10,30,35]. Finding effective logistic ways to ensure adherence to guidelines might enhance the effectiveness of follow-up.

A further reason to omit CEA from follow-up that was mentioned by several surgeons in this survey was that a normal preoperative CEA would mean that it will not rise when recurrence occurs. This, however, is not valid. A normal preoperative CEA is present in approximately 50% of all patients with rectal carcinoma, and 50% will rise with recurrent disease. Thus 25% will miss a chance of early detection when CEA follow-up is omitted (I. Grossmann e.a., *EJSO* 2007; 33: 183–187).

A majority of surgeons added ultrasound as a screening tool in their follow-up, though this was not included in the national guidelines. This may be because one regional guideline advises ultrasound when preoperative CEA is normal. Another reason might be low confidence in the value of CEA as a tumour marker, and the increasing confidence in imaging. In recent years major advances have been made in imaging. The present multi-slice helical CT scan can detect liver and lung metastasis when its diameter exceeds approximately 0.5 cm. It is feasible therefore to localize recurrent disease in lung and liver as soon as CEA exceeds its threshold [15,27,36]. Thus a major problem in the past has finally been solved. When CEA rises, recurrent disease can nowadays usually be localized and, where feasible, treatment can be initiated immediately. The ability of ultrasound examination to detect liver metastasis is less sensitive. Evaluation is limited to the liver, while lung metastases are also frequently curable. Considering this, the role of regular hepatic ultrasound in follow-up is questionable when helical CT scanning of thorax and abdomen is available instead. The frequency of performing a CT scan however, is limited by availability, cost and the potential health risk of radiation exposure.

More patients seem eligible for surgical treatment of metastatic disease than appear to be eligible in the Netherlands. Uncertainty exists regarding the criteria for liver resection for metastasis, as also shown in another recent Dutch survey [37]. The difference of opinion

between liver surgeons and general surgeons on some criteria might be an expression of this finding. In the last 10 years many criteria, that were previously considered contra-indications for metastasectomy, are now being debated. Among these criteria are age, number and localization of metastasis, presence of resectable extrahepatic disease and previous metastasectomy. The increasing safety and technical advancements have resulted in more older patients becoming candidates for metastasectomy. Furthermore, many patients with disseminated colorectal carcinoma are relatively young at 60–65 years. The number and involvement of multiple segments of both liver and lung are not contraindications, provided they are completely resectable [32,34,38–41] although the Dutch general surgeons in the survey often considered the metastasis count of liver metastasis (23.5%) and bilobar involvement (18%) to prohibit resection. Resection of synchronous or metachronous lung metastases may result in long-term survival equal to resectable metastasis confined to only one organ [33,34,42–44]. Among the Dutch surgeons 8–12% did not consider these patients eligible for surgery. Re-resection of metastases of both lung and liver result in near equal survival rates as after the first metastasectomy [32,34,39–45]. The differences in opinion regarding eligibility for hepatic metastasectomy indicate ongoing advances in liver surgery, which allow more patients to be a candidate for curative surgery. The same appears to be true for lung metastasis.

There is considerable controversy about follow-up after curative treatment of colorectal carcinoma because it has thus far not been proven to increase survival or quality of life. Meanwhile, recent rapid technical developments in imaging and advances in liver and lung surgery have changed the circumstances. Review of the guidelines on follow-up to reflect these changes is required. The high motivation among Dutch surgeons to participate in a new study appears to support this, making a national trial feasible.

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